

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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KJ

In re PATENT APPLICATION OF  
WEINBERG et al

Serial No.: 08/753,851

Filed; December 2, 1996



Atty. Ref.: 1579-21

Group Art Unit: 1644

Examiner: Gambel

For: **METHOD OF INHIBITING HIV INFECTION**

\* \* \* \* \*

**DECLARATION**

Hon. Commissioner of Patents and Trademarks

Washington, DC 20231

Sir:

I, Kent Weinhold, do hereby declare and state as follows:

1. I hold the position of Professor with tenure in the Department of Surgery and Associate Professor in the Department of Immunology at Duke University, Durham, North Carolina. I have held these positions for one and two years, respectively.
2. From September 1984 through present day, the major portion of my research efforts have been focused on the Human Immunodeficiency Virus type 1 (HIV-1). These efforts have included: (1) pre-clinical development of anti-retroviral drugs, (2) development, immunologic testing and clinical evaluation of preventive AIDS vaccine strategies and (3) various aspects of HIV-1 immunopathogenesis. A copy of my curriculum vitae is attached.
3. I have reviewed the disclosure and claims of the above-identified application. I have also reviewed the Office Action dated September 8, 1999, and thus I am aware that the Examiner has taken the position that, in 1991, it would not have been predictable on the basis of the data provided in the application that targeting CD44 in mononuclear phagocytes would affect

HIV infection in a patient. The Examiner also appears to have taken the view that the application does not include sufficient detail to have permitted one to actually use the treatment method claimed. I respectfully disagree for the reasons set forth below.

4. The invention described and claimed in the above application results from Applicants' finding that CD44 (the hyaluronate receptor) facilitates HIV infection in human cells. Applicants report in the application that when CD44 is blocked by binding to an anti-CD44 antibody, there is a 40-80% reduction of HIV infection/expression in human monocytes and tissue macrophages *in vitro*. Applicants also report that the natural ligand of CD44, hyaluronate or hyaluronic acid, inhibits infection/expression up to 85%. In contrast, chondroitin sulfate, a polyanion that does not bind CD44, reportedly has little if any inhibitory activity.

The Examiner states in the September 8 Office Action that it was well known that cellular CD4 is the predominant membrane protein that interacts with HIV. Indeed, Applicants acknowledge in their application that *in vitro* studies had demonstrated that HIV infects human lymphocytes and mononuclear phagocytes by way of adherence of the virus gp120 to cellular membrane CD4. Applicants point out, however, that while anti-CD4 antibodies block HIV infection, this is usually not complete and that auxiliary cellular receptors and pathways for HIV infection had been postulated but not demonstrated. Based on Applicants' data, CD44 is one such auxiliary cellular pathway.

The ability to block HIV infection of mononuclear phagocytes using CD44 blocking agents is of obvious significance. Human mononuclear phagocytes (monocytes and macrophages) are critical cells in the initial phase of HIV infection *in vivo*, and in the spread of infection from cell-to-cell once infection is established. Most new infections involve preferential infection with monocytotropic (non-syncytium-inducing) strains of HIV. Researchers have noted the critical importance of mononuclear phagocytes and monocytotropic strains of HIV in the transmission and spread of HIV infection. Despite the existence of several different quasi-species of HIV in infected individuals, monocytotropic strains are preferentially transmitted *in vivo* to mononuclear phagocytes (see citations 1 and

2—copies attached). The virus infects monocytes and macrophages along paths of infection, and these cells are critical for spread of the virus throughout the body. Strategies using anti-CD44 treatments would therefore target these critically important cell types. Mononuclear phagocytes are concentrated in the mucosa (for example, the vaginal and bowel mucosa) and thus are important target cells. Fortunately, from a therapeutic standpoint, these target cells are readily accessible. That is, the CD44 blocking agent can be administered topically to the mucosal surface or, for example, within a condom. In this regard, the application makes specific reference to loco-regional (for example, intravaginal) administration. Alternatively, the blocking agent can be administered parenterally.

5. The concept underlying the invention is a straightforward one. That being the case, I see little reason to doubt the effectiveness of the approach, given the results obtained *in vivo* and described in the application. I am aware, as indicated above, that the Examiner has a different view but I do not find anything in the September 8, 1999 Office Action that would provide basis for the Examiner's skepticism.

The strategy proposed by Applicants can be expected to be effective for several reasons.

(a) These treatments would target a novel pathway, the CD44-hyaluronate path. No other anti-HIV treatments are directed to this. (b) The treatments would be aimed at the most important cell for primary infection with HIV and for spread of the infection *in vivo* (the mononuclear phagocyte). (c) There are numerous examples of successful use of antibody or soluble receptor therapy in human disease. This includes use of anti-tumor necrosis factor antibody or soluble receptor for treatment of inflammatory diseases such as rheumatoid arthritis or inflammatory bowel disease (see citations 3-5—copies attached). Likewise, anti-CD44 antibody has been successfully used to reduce inflammation in mice with arthritis (see citation 6—copy attached). Thus, there is good precedent to indicate that these strategies will be useful in treatment of HIV infection in humans.

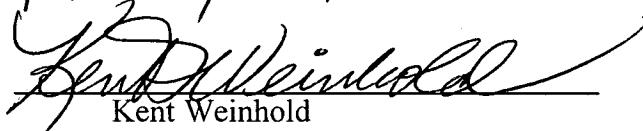
6. Many different standard techniques could be used to identify agents (other than those specifically described in the application) that could be used to block CD44 (and thus block HIV infection). Among these standard techniques are (a) enzyme-linked microplate assays to

assess binding of agents to solid phase CD44, and (b) flow cytometric measurement of CD44-specific binding to CD44-expressing cells. These assays are in routine use and have been since April of 1991, and they lend themselves to high throughput screening procedures.

I hereby declare that all statements made herein of my knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Further, declarant sayeth not.

Signed this 28th day of February, 2000



Kent Weinhold

**Citations:**

1. Zhu, T., H. Mo, N. Wang, D.S. Nam, Y. Cao, R.A. Koup, and D.D. Ho. 1993. Genotypic and phenotypic characterization of HIV-1 patients with primary infection. *Science* 261:1179-81.
2. Wolinsky, S.M., C.M. Wike, B.T. Korber, C. Hutto, W.P. Parks, L.L. Rosenblum, K.J. Kunstman, M.R. Furtado, and J.L. Munoz. 1992. Selective transmission of human immunodeficiency virus type-1 variants from mothers to infants [see comments]. *Science* 255:1134-7.
3. Elliott, M.J., R.N. Maini, M. Feldmann, J.R. Kalden, C. Antoni, J.S. Smolen, B. Leeb, F.C. Breedveld, J.D. Macfarlane, H. Bijl, and et al. 1994. Randomised double-blind comparison of chimeric monoclonal antibody to tumour necrosis factor alpha (cA2) versus placebo in rheumatoid arthritis. *Lancet* 344:1105-10.
4. Sandborn, W.J., and S.B. Hanauer. 1999. Antitumor necrosis factor therapy for inflammatory bowel disease: A review of agents, pharmacology, clinical results, and safety [Review]. *Inflammatory Bowel Diseases* 5:119-133.
5. Cooksey, L.J. 1999. Enbrel: A TNF-receptor blocker for treating patients with refractory rheumatoid arthritis. *Hospital Formulary* 34:211-+.
6. Mikecz, K., F.R. Brennan, J.H. Kim, and T.T. Glant. 1995. Anti-CD44 treatment abrogates tissue oedema and leukocyte infiltration in murine arthritis. *Nature Med.* 1:558-63.

## **CURRICULUM VITAE**

### **Kent James Weinhold**

#### **PERSONAL DATA**

##### **Major Areas of Expertise:**

Human Cellular Immunology  
Anti-Viral and Anti-Tumor Immunity  
Vaccines  
AIDS Pathogenesis

##### **Professional Address:**

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##### **Home Address:**

1320 Arnette Avenue  
Durham, North Carolina 27707-1602  
Phone: (919) 489-6613

##### **Social Security Number:**

180-38-0329

##### **Date & Place of Birth:**

March 14, 1949  
Ephrata, Pennsylvania

##### **Marital Status:**

Married

##### **Spouse:**

Adele M.

##### **Children:**

Kristin E., Andrew K.

#### **ACADEMIC TRAINING**

##### **Ph.D.**

Microbiology, Thomas Jefferson University,  
Philadelphia, PA 19107 (1979)  
Dissertation: "The Immunologic Basis of the L5178Y  
Tumor Dormant State Established in Syngeneic Murine Hosts."  
Professor: Dr. E.F. Wheelock

M.S.	<u>Clinical Microbiology</u> , Thomas Jefferson University, Philadelphia, PA 19107 (1974) <u>Research Project</u> : "An Indirect Immunofluorescent Technique for the Detection of Serum Antibody to <i>Neisseria Gonorrhoeae</i> ." <u>Professor</u> : Dr. R.W. Schaedler and Dr. J.M. Clark
B.S.	<u>Microbiology</u> , Pennsylvania State University, University Park, PA 16802 (1971)

### PROFESSIONAL EXPERIENCE

Jan.15, 1999- Present	Professor of Surgery (with tenure) Department of Surgery Duke University Medical Center
July 1, 1997 - Present	Associate Professor of Immunology Department of Immunology Duke University
May, 1997 - Present	Chairman Immunology Committee AIDS Vaccine Evaluation Group: NIAID/NIH
July 1, 1996 - July, 1997	Assistant Professor of Immunology Department of Immunology Duke University
March, 1991 - Present	Chief Cellular Immunologist Central Immunology Laboratory AIDS Vaccine Evaluation Group: NIAID/NIH
March, 1991 - July, 1993	Vice-Chairman Immunology Core Committee AIDS Clinical Trials Group: NIAID/NIH
Nov., 1989 - July, 1993	Co-Chairman Immune Based Therapies Committee AIDS Clinical Trials Group: NIAID/NIH
Sept., 1989 - Present	Director Cellular Immunology Program Duke Center for AIDS Research (CFAR): NIAID/NIH

Feb., 1989 – Jan. 15, 1999	Associate Professor of Experimental Surgery Department of Surgery Duke University Medical Center
May, 1988 - March, 1991	Protocol Chairman ACTG Therapy Protocol 042.1 (Phase 1) Combined AZT/IL-2 Therapy of AIDS AIDS Treatment Evaluation Unit: NIAID/NIH Duke University Medical Center
Jan., 1987 - July, 1993	Chief Cellular Immunologist AIDS Treatment Evaluation Unit: NIAID/NIH Duke University Medical Center
Jan., 1987 - July, 1993	Chief Retrovirologist AIDS Treatment Evaluation Unit: NIAID/NIH Duke University Medical Center
Sept., 1986 - July, 1990	Chief Retrovirologist National Cooperative Drug Discovery Group: NIAID/NIH Duke University Medical Center
July, 1986 - July, 1991	Project Leader (Co-Investigator) Pre-Clinical Studies on Prevention and Intervention in AIDS: NCI/NIH Duke University Medical Center
July, 1982 - Feb., 1989	Assistant Medical Research Professor Department of Surgery Duke University Medical Center
Nov., 1981 - July, 1982	Associate Department of Surgery Duke University Medical Center
July, 1980 - Nov., 1981	Post-doctoral Research Associate Laboratory of Dr. D.P. Bolognesi Duke University Medical Center
July, 1980 - July, 1982	Post-doctoral Trainee Division of Immunology Duke University Medical Center
June, 1979 - July, 1980	Post-doctoral Research Associate Laboratory of Dr. E.F. Wheelock Thomas Jefferson University

1976 - 1979	Teaching Assistant, Immunology College of Allied Health Sciences Thomas Jefferson University
1975 - 1979	University Teaching Assistant College of Allied Health Sciences Thomas Jefferson University
1974 - 1978	Laboratory Assistant, Microbiology Jefferson Medical College Thomas Jefferson University
1974 - 1977	Laboratory Instructor, Microbiology College of Allied Health Sciences Thomas Jefferson University
1974	Co-coordinator, Workshop on Fluorescent Antibody Techniques Microbiology Pennsylvania State University

#### PROFESSIONAL SOCIETIES

- American Association for the Advancement of Science (AAAS)
- American Association of Immunologists
- American Federation for Clinical Research
- American Association for Cancer Research
- Clinical Immunology Society
- Duke University Comprehensive Cancer Center
- Sigma Xi
- Society for Biological Therapy

#### AWARDS

1994	Thomas Jefferson University CGS Distinguished Alumnus Award
1980 - 1982	NCI Post-Doctoral Traineeship Award
1979	Sigma Xi Student Research Award

#### REVIEWER (AD HOC)

AIDS Research and Human Retroviruses, Clinical Laboratory Immunology, Journal of Clinical Investigation, Journal of Infectious Diseases, Journal of Immunology, Journal of Virology, Proceedings of the National Academy of Science (USA), Science.

REVIEW COMMITTEES

Member

Special Emphasis Panel to Review Unsolicited Applications  
National Institute of Allergy and Infectious Diseases, NIH  
1996-1999

Chairman

Ad Hoc Review Committee  
RFP NIH-NIAID-96-03  
June, 1995

Member

Veterans Administration  
Infectious Diseases Merit Review Board  
July, 1992 - June, 1995

Member

Clinical Applications, Prevention, and Treatment Subcommittee  
AIDSRRCC  
National Institute of Allergy and Infectious Diseases, NIH  
July, 1990 - June, 1995

Member

AIDS Advisory Committee  
National Institute of Environmental Health Sciences, NIH  
November, 1987 - 1988

RFP-NIH-NCI-PRI-S87-77

NCI, Frederick Cancer Research Facility, NIH  
July 23, 1987

Study Section Reviewer

RFP-NIH-NIAID-AIDSP-87-12  
National Institute of Allergy and Infectious Diseases, NIH  
February 11, 1987

Study Section Reviewer

RFP-NIH-NIAID-MIDF-87-3  
National Institute of Allergy and Infectious Diseases, NIH  
May 8, 1986

### CURRENT RESEARCH SUPPORT

1996 - 2001      Host-Virus Interactions During Acute HIV-1 Infection  
                    National Institute of Allergy and Infectious Diseases (1PO1AI40237)  
                    Co-Principal Investigator

1996 - 2002      Central Immunology Laboratory for AIDS Vaccine Clinical Trials  
                    National Institute of Allergy and Infectious Diseases (1N01AI65305)  
                    Co-Investigator

1995 - 1999      Analysis of Anti-HIV CTL & HIV Suppressive CD8<sup>+</sup> Cells  
                    National Institute of Allergy and Infectious Diseases (2R01AI29852)  
                    Principal Investigator

1995 - 1999      Viral Control and Immune Reconstitution in HIV Infection (SPIRAT)  
                    National Institute of Allergy and Infectious Diseases (5U01AI38587)  
                    Co-Investigator: Core 2

1995 - 2001      SPORE in Breast Cancer  
                    National Cancer Institute (1P50CA68438)  
                    Project 5 - Co-Principal Investigator

### PAST RESEARCH SUPPORT

1992 - 1997      Molecularly Defined TAA as Human Anti-Tumor CTL Targets  
                    National Cancer Institute (1R01CA58005)  
                    Principal Investigator

1991 - 1996      Central Immunology Laboratory for AIDS Vaccine Clinical Trials  
                    National Institute of Allergy and Infectious Diseases (1N01AI5106)  
                    Co-Investigator

1991 - 1995      Pre-Clinical Studies on Prevention & Intervention in AIDS  
                    National Cancer Institute (1PO1CA43447)  
                    Co-Investigator

1990 - 1995      Characterization of Anti-HIV-1 Cellular Cytotoxicities  
                    National Institute of Allergy and Infectious Diseases (1R01AI29852)  
                    Principal Investigator

1989 - 1994      Duke University Center for AIDS Research (CFAR)  
                    National Institute of Allergy and Infectious Diseases (5 P30AI28662)  
                    Co-Investigator

1988 - 1991	Duke/DuPont Collaborative Research Pre-Clinical Studies of LAK Cell Therapy of AIDS Principal Investigator
1988 - 1990	Duke/Burroughs Wellcome Collaborative Research Burroughs Wellcome Principal Investigator
1986 - 1991	The Establishment of an AIDS Treatment Evaluation Unit National Institute of Allergy and Infectious Diseases (5U01A127662) Co-Investigator
1986 - 1992	Treatment of AIDS and AIDS Related Complex Veterans Administration Contract #298 Co-Investigator
1986 - 1991	Nucleoside and Oligonucleotide Analogs for AIDS Therapy NCDDG for Treatment of AIDS National Institute of Allergy and Infectious Diseases (1U01CA44082) Co-Investigator
1986 - 1991	Pre-Clinical Studies on Prevention and Intervention in AIDS National Cancer Institute (5P01CA43447) Co-Investigator
1987 - 1991	Hepatopoietins, Liver Regeneration and Carcinogenesis National Cancer Institute (5R01CA35373) Co-Investigator
1986 - 1988	Development of Anti-HTLV-III Specific Agents and Treatment Approaches (Contract #FOD-0759; Task III), FCRC (NIH) Principal Investigator
1986 - 1988	Characterization of the Human Immune Response to HTLV-III (Contract #FOD-0758; Task II), FCRC (NIH) Co-Investigator
1983 - 1986	Passive Immunotherapy of Spontaneous AKR Leukemia National Cancer Institute (R01CA33387) Principal Investigator
1983 - 1986	Hepatopoietins, Liver Regeneration and Carcinogenes National Cancer Institute (1R01CA35373) Co-Investigator
1983 - 1985	Control of Neoplasia by Passive Serum Therapy National Cancer Institute (5P01CA25863) Associate

## PUBLICATIONS

1. Wheelock, E.F., Goldstein, L.T., **Weinhold, K.J.**, Carney, W.P. and Marx, P.A. The tumor dormant state. In: Cancer Invasion and Metastasis, S.B. Day, Ed., Raven Press, pp. 105-116, 1977.
2. **Weinhold, K.J.**, Goldstein, L.T. and Wheelock, E.F. Tumor-dormant states established with L5178Y lymphoma cells in immunized syngeneic murine hosts. Nature 270:59-61, 1977.
3. Wheelock, E.F., Carney, W.P. and **Weinhold, K.J.** Murine models of tumor dormancy. In: Adv. in Comparative Leukemia Res., Proceedings of the VIIth International Symposium on Comparative Research on Leukemia and Related Diseases. Elsevier/North Holland, Biomedical Press, pp. 123-129 1978.
4. Clark, J.M. and **Weinhold, K.J.** Infection of artificial pouches in the connective tissue of mice with *Neisseria gonorrhoeae*. J. Med. Microbiology 12:233-237, 1979.
5. **Weinhold, K.J.**, Miller, D.A. and Wheelock, E.F. The tumor dormant state: Comparison of L5178Y cells used to establish dormancy with those that emerge after its termination. J. Exp. Med. 149:745-757, 1979.
6. **Weinhold, K.J.**, Goldstein, L.T., and Wheelock, E.F. The tumor dormant state: Quantitation of L5178Y cells and host immune responses during the establishment and course of dormancy in syngeneic DBA/2 mice. J. Exp. Med. 149:732-744, 1979.
7. Wheelock, E.F., **Weinhold, K.J.**, and Goldstein, L.T. Tumor dormancy in animals and man. In: Cancer Metastasis, E. Grundmann, Ed., Springer-Verlag, New York and Heidelberg, 1980.
8. Wheelock, E.F., **Weinhold, K.J.**, Ingenito, G.G. and Goldstein, L.T. *In vivo* lysis of L5178Y cells in the establishment of the tumor-dormant state in DBA/2 mice. J. Immunol. 124:1642-1647, 1980.
9. Wheelock, E.F., **Weinhold, K.J.**, and Levich, J.D. The tumor dormant state. Adv. in Cancer Res. 34:107-139, 1981.
10. Iglehart, J.D., **Weinhold, K.J.**, Huper, G., Thiel, K. and Bolognesi, D.P. *In vivo* antigenic modification of tumor cells. III. Metastatic thymic lymphoma specifically infected by thymotropic retrovirus. J. Natl. Cancer Inst. 67:123-130, 1981.
11. Thiel H.J., Matthews, T.J., Broughton, E.M., **Weinhold, K.J.**, Bolognesi, D.P., Graf, T., and Beug, H. Clonal isolate of the simian sarcoma virus codes for a gag-related 65,000 dalton protein. Virology 114:124-131, 1981.
12. Thiel H.J., Matthews T.J., **Weinhold K.J.**, and Broughton E.M. Identification of a 20,000 dalton protein in SSV-transformed non- producer cells. Virology 115:401-405, 1981.

13. Fischinger, P.J. Dunlop, N.M., Schwarz, H., Ihle, J.N., **Weinhold, K.J.**, Bolognesi, D.P. and Schafer W. Properties of mouse leukemia viruses. XVIII. Effective treatment of AKR leukemia with antibody to gp71 eliminates the neonatal burst of ecotropic AKR virus- producing cells. *Virology* 119:68-81, 1982.
14. Ward, E.C., Iglehart, J.D., **Weinhold, K.J.**, and Bolognesi, D.P. Immunotherapy of an MuLV infected chemically-induced murine sarcoma with anti-viral antibodies. *J. Natl. Cancer Inst.* 69:509-515, 1982.
15. Thiel, H.J., Weiland, F., Matthews, T.J. and **Weinhold, K.J.** Intracellular cleavage of an SSV coded gag-related protein. *Virology* 123:229-234, 1982.
16. **Weinhold, K.J.** and Wheelock, E.F. Cross-reacting antigens on L5178Y cells which serve as targets for cytotoxic T-lymphocytes during establishment of the tumor dormant state. *Cancer Res.* 42:3607-3616, 1982.
17. Matthews, T.J., Langlois, A.J., **Weinhold, K.J.**, and Bolognesi, D.P. Differential tumocidal activity of murine IgG isotypes administered either alone or in combination with thioglycollate and *C. parvum*. *Hybridoma* 2:120, 1983.
18. Iglehart, J.D., **Weinhold, K.J.**, Ward, E.C., Matthews, T.J., Langlois, A.J., Schafer, W. and Bolognesi, D.P. Prospects for the immunological management of lethal tumors. *J. Cancer Invest.* 1(5):409-421, 1983.
19. **Weinhold, K.J.**, Huper, G., Matthews, T.J., Fischinger, P.J., Ihle, J.N., Schwarz, H., Thiel, H.-J., Schafer, W. and Bolognesi, D.P. Properties of Mouse Leukemia Viruses XIX. Effective antibody therapy of AKR leukemia occurs independently of virus neutralization and produces long-term changes in the virus status of the thymus. *Virology* 135:105-117, 1984.
20. Schwarz, H., Thiel, H.-J., **Weinhold, K.J.**, Bolognesi, D.P. and Schafer, W. Stimulation of immunoreactivity against endogenous retroviruses and protection against leukemia of older AKR mice by treatment with antibodies against retroviral surface components. Role of p15(E) antibody. *Naturforsch.* 39c 1199-1202, 1984.
21. Langweiler, M., **Weinhold, K.J.**, Matthews, T.J. and Bolognesi, D.P. *In vitro* antigenic modification of tumor cells: Effect on susceptibility to natural cell-mediated cytotoxicity. *J. Natl. Cancer Inst.* 74:699-704, 1985.
22. Matthews, T.J., **Weinhold, K.J.**, Langlois, A.J. and Bolognesi, D.P. Immunologic control of a retrovirus associated murine adenocarcinoma. VI. Augmentation of antibody dependent killing following quantitative and qualitative changes in host peritoneal cells. *J. Natl. Cancer Inst.* 75:703-708, 1985.
23. Langlois, A.J., Matthews, T.J., **Weinhold, K.J.**, and Bolognesi, D.P. Immunologic control of a retrovirus associated murine adenocarcinoma. VII. Tumor cell destruction by macrophages and IgG<sub>2A</sub>. *J. Natl. Cancer Inst.* 75:709-715, 1985.

24. **Weinhold, K.J.**, Bolognesi, D.P. and Matthews, T.J. Immunologic control of a retrovirus associated-murine adenocarcinoma. VIII. C. parvum activated NK cells as potent ADCC effectors. J. Natl. Cancer Inst. 75:717-724, 1985.
25. Mitsuya, H., **Weinhold, K.J.**, Nusinoff-Lehrman, S., Gallo, R.C., Bolognesi, D.P., Barry, D.W. and Broder, S.K. 3'-azido-3'deoxythymidine (BW-A509U): A new antiviral agent that inhibits the infectivity and cytopathic effect of human T-lymphotropic virus type III/lymphadenopathy-associated virus *in vitro*. Proc. Natl. Acad. Sci. (USA) 82:7096-7100, 1985.
26. Schwarz, H., Thiel, H.-J., **Weinhold, K.J.**, Fischinger, P.J., Bolognesi, D.P. and Shafer, W. Properties of Mouse Leukemia Viruses XX. Variation of AKR substrains in response to antibody therapy. Virology 150:247-251, 1986.
27. White, G.C., II, Matthews, T.J., **Weinhold K.J.**, Haynes, B.F., Cromartie, H.L., McMillan, C.W. and Bolognesi, D.P. HTLV-III seroconversion associated with heat-treated factor VIII concentrate. Lancet (March)611-612, 1986.
28. Yarchoan, R., Klecker, R.W., **Weinhold, K.J.**, Markham, P.D., Lyerly, H.K., Durack, D.T., Gelmann, E., Lehrman, S.N., Blum, R., Barry, D.W., Shearer, G.M. Fisch, M.A., Mitsuya, H., Gallo, R.C., Collins, J.C., Bolognesi, D.P., Myers, C.E. and Broder, S. The administration of 3'-Azido-3'deoxythymidine, an inhibitor of HTLV/LAV replication, to patients with AIDS or AIDS-related complex. Lancet (March)575-580, 1986.
29. Lyerly, H.K., **Weinhold, K.J.**, Cohen, O.C. and Bolognesi, D.P. Defects in T cell function after infection with HTLV-III/LAV. Surg. Forum 37:405-407, 1986.
30. Furman, P.A., Fyfe, J.A., St. Clair, M.H., **Weinhold, K.J.**, Rideout, J.L., Mitsuya, H. and Barry, D.W. Phosphorylation of 3'-azido-3'deoxythymidine and selective interaction of the 5'-triphosphate with human immunodeficiency virus reverse transcriptase. Proc. Natl. Acad. Sci. (USA) 83:8333-8337, 1986.
31. Putney, S.D., Matthews, T.J., Robey, W.G., Lynn, D.L., Robert-Guroff, M., Mueller, W.T., Langlois, A.J., Ghrayeb, J., Petteway, S.R., Jr., **Weinhold, K.J.**, Fischinger, P.J., Wong-Staal, F., Gallo, R.C. and Bolognesi, D.P. HTLV-III/LAV-neutralizing antibodies to an *E. coli* produced fragment of the virus envelope. Science 234:1392-1395, 1986.
32. Lyerly, H.K., **Weinhold, K.J.**, and Bolognesi, D.P. Surgical aspects of viral hepatitis and acquired immunodeficiency syndrome. In: Essentials of Surgery, D.C. Sabiston, Ed., W.B. Saunders, Philadelphia, pp. 169-179, 1987.
33. Matthews, T.J., **Weinhold, K.J.**, Lyerly, H.K., Langlois, A.J., Wigzell, H. and Bolognesi, D.P. Interaction between the human T-cell lymphotropic virus type III<sub>B</sub> envelope gp120 and the surface antigen CD4: Role of carbohydrate in binding and cell fusion. Proc. Natl. Acad. Sci. (USA) 84:5424-5428, 1987.

34. Lyerly, H.K., Cohen, O.J. and **Weinhold, K.J.** Transmission of HTLV-III by antigen presenting cells during T-cell activation: Prevention by 3'-azido-3'-deoxythymidine. AIDS Res. Hum. Retroviruses 3:87-94, 1987.
35. Lyerly, H.K., Matthews, T.J., Langlois, A.J., Bolognesi, D.P. and **Weinhold, K.J.** Human T-cell lymphotropic virus III<sub>B</sub> glycoprotein (gp120) bound to CD4 determinants on normal lymphocytes and expressed by infected cells serves as target for immune attack. Proc. Natl. Acad. Sci. (USA) 84:4601-4605, 1987.
36. Buckheit, R.W. Jr., Bolognesi, D.P. and **Weinhold, K.J.** The effects of leukemosuppressive immunotherapy on bone marrow infectious cell centers in AKR mice. Virology 157:387-396, 1987.
37. Matthews, T.J., Lyerly, H.K., **Weinhold, K.J.**, Langlois, A.J., Putney, S.D. and Bolognesi, D.P. Prospect for development of a vaccine against HTLV-III related disorders. Clinical Immunology Newsletter 8:49-52, 1987.
38. Kurtzberg, J., Friedman, H.S., Stine, K.C., Chaffee, S., Kinney, T.R., Falletta, J.M. and **Weinhold, K.J.** Management of human immunodeficiency virus associated thrombocytopenia with intravenous gamma globulin. Am. J. Ped. Hematology/Oncology 9:299-301, 1987.
39. St. Clair, M. Richards, C, Spector, T., **Weinhold, K.**, Miller, W. Langlois, A. and Furman, P.A. 3'-azido-3'-deoxythymidine triphosphate as an inhibitor and substrate of purified human immunodeficiency virus reverse transcriptase. Antimicrob. Agents Chemother. 31:1972-1977, 1987.
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